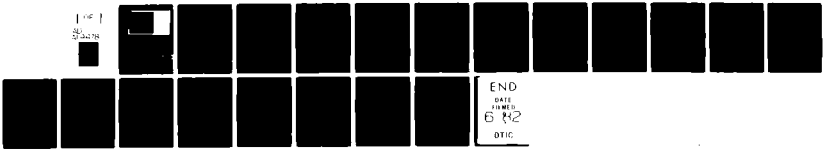
AD-A114 478 WISCONSIN UNIV-MADISON MATHEMATICS RESEARCH CENTER F/G 6/5
ASSESSING SENSITIVITY TO AN UNOBSERVED BINARY COVARIATE IN A NO--ETC(U)
JAN 82 P R ROSENBAUM, D B RUBIN DAAG29-80-C-0041
UNCLASSIFIED MRC-TSR-2321 NL



END
DATE FILMED
6 82
DTIC

MRC Technical Summary Report # 2321

# ASSESSING SENSITIVITY TO AN UNOBSERVED BINARY COVARIATE IN A NONRANDOMIZED EXPERIMENT WITH BINARY OUTCOME

Paul R. Rosenbaum
and
Donald B. Rubin

**Mathematics Research Center**
**University of Wisconsin—Madison**
**610 Walnut Street**
**Madison, Wisconsin 53706**

January 1982

(Received November 9, 1981)



**Approved for public release**
**Distribution unlimited**



Sponsored by

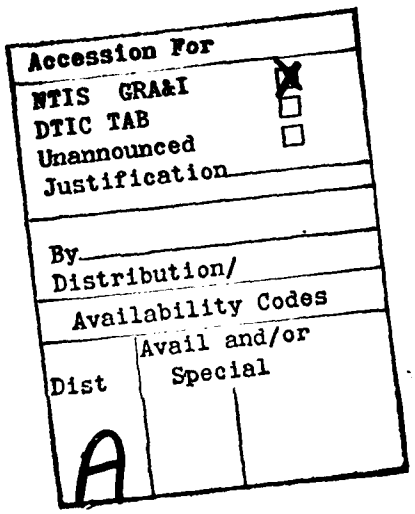
U. S. Army Research Office
P. O. Box 12211
Research Triangle Park
North Carolina 27709

National Cancer Institute
9000 Rockville Pike
Bethesda, MD 20205

Health Resources
Administration
3700 East-West Highway
Hyattsville, MD 20782

ACKNOWLEDGEMENT

The authors wish to acknowledge valuable discussions with Arthur P. Dempster and Roderick J. A. Little on the subject of this paper.




UNIVERSITY OF WISCONSIN - MADISON
MATHEMATICS RESEARCH CENTER

# ASSESSING SENSITIVITY TO AN UNOBSERVED BINARY COVARIATE IN A NONRANDOMIZED EXPERIMENT WITH BINARY OUTCOME

Paul R. Rosenbaum* and Donald B. Rubin**

Technical Summary Report #2321

January 1982

ABSTRACT

The results of nonrandomized clinical experiments are often disputed because patients at greater risk may be overrepresented in some treatment groups. This paper proposes a simple technique providing insight into the range of plausible conclusions from a nonrandomized experiment with binary outcome and observed categorical covariate. The technique assesses the sensitivity of conclusions to assumptions about an unobserved binary covariate relevant to treatment assignment, and is illustrated in a medical study of coronary artery disease.

AMS (MOS) Subject Classification: 62P99, 62J05, 62F12, 62F11

Key Words: Observational studies, sensitivity analysis, categorical data.

Work Unit Number 4 - Statistics and Probability

---

* Assistant Professor, Departments of Statistics and Human Oncology, University of Wisconsin-Madison.

** Visiting Professor, Mathematics Research Center, University of Wisconsin-Madison.

---

This work was partially supported by Health Resources Administration contract HRA 230-76-0300, partially by the Division of Statistics and Applied Mathematics, Office of Radiation Programs, U. S. Environmental Protection Agency, partially by grant P30-CA-14520 from the National Cancer Institute to the Wisconsin Clinical Cancer Center, and partially sponsored by the U. S. Army Research Office under Contract No. DAAG29-80-C-0041.

# ASSESSING SENSITIVITY TO AN UNOBSERVED BINARY COVARIATE IN A NONRANDOMIZED EXPERIMENT WITH BINARY OUTCOME

Paul R. Rosenbaum* and Donald B. Rubin**

## 1. INTRODUCTION AND NOTATION

Inevitably, the results of clinical experiments are subject to dispute. In nonrandomized experiments, one basis for dispute is obvious: since patients were not assigned to treatments at random, patients at greater risk may be overrepresented in some treatment groups. This paper proposes a method for assessing the sensitivity of conclusions to an unmeasured patient characteristic relevent to treatment assignment. Despite their limitations, nonrandomized experiments will continue to be performed, and therefore it is prudent to develop appropriate methods of analysis for them.

Our sensitivity analysis consists of the estimation of the average effect of a treatment on a binary outcome variable after adjustment for observed categorical covariates and an unobserved binary covariate $u$, under several sets of assumptions about $u$. Both Cornfield, et. al (1959) and Bross (1966) have proposed guidelines for determining whether an unmeasured binary covariate having specified properties could explain all of the apparent effect of a treatment; i.e., whether the treatment effect, after adjustment for $u$, could be zero. Our method has two advantages: first, Cornfield, et. al.

---

* Assistant Professor, Departments of Statistics and Human Oncology, University of Wisconsin-Madison.

** Visiting Professor, Mathematics Research Center, University of Wisconsin-Madison.

This work was partially supported by Health Resources Administration contract HRA 230-76-0300, partially by the Division of Statistics and Applied Mathematics, Office of Radiation Programs, U. S. Environmental Protection Agency, partially by grant P30-CA-14520 from the National Cancer Institute to the Wisconsin Clinical Cancer Center, and partially sponsored by the U. S. Army Research Office under Contract No. DAAG29-80-C-0041.

(1959) and Bross (1966) adjust only for the unmeasured covariate u, whereas we adjust for measured covariates in addition to the unmeasured covariate u; second, Cornfield, et. al. (1959) and Bross (1966) only judge whether the effect of the treatment could be zero having adjusted for u, whereas we provide an actual estimate of the treatment effect adjusted for u as well as the observed categorical covariates.

In principle, the $i^{th}$ of the N patients under study has both a binary response $r_{1i}$ that would have resulted if he had received the new treatment, and a binary response $r_{0i}$ that would have resulted if he had received the control treatment. In this formulation, treatment effects are comparisons of $r_{1i}$ and $r_{0i}$, such as $r_{1i} - r_{0i}$. Since each patient receives only one treatment, either $r_{1i}$ or $r_{0i}$ is observed, but not both. Therefore, comparisons of $r_{1i}$ and $r_{0i}$ imply some degree of speculation. Treatment effects defined as comparisons of the two potential responses, $r_{1i}$ and $r_{0i}$, of individual patients are implicit in Fisher's (1953) randomization test of the sharp null hypothesis that $r_{1i} = r_{0i}$, $i = 1,\ldots,N$. Such definitions are used explicitly by Kempthorne (1952) in his discussion of randomization based inference, and by Rubin (1977, 1978), Hamilton (1979), and Rosenbaum and Rubin (1981) in discussions of observational studies. (The definition does contain some implicit assumptions, such as the assumption of noninterference between patients; see Cox (1958, chapter 2) or Rubin (1978, section 2.3) for discussion.) Here, the N patients in the study are viewed as a simple random sample from some population, and the average treatment effect is defined as

$$E(r_1) - E(r_0) = \text{prob}(r_1 = 1) - \text{prob}(r_0 = 1) = \tau_1 - \tau_2, \text{ say} \qquad (1.1)$$

where $E(\cdot)$ and $\text{prob}(\cdot)$ denote expectation and probability, respectively, in the population.

For the $i^{th}$ patient of $N$ patients in the study $(i = 1,\ldots,N)$ let $z_i$ be the indicator for treatment assignment, and let $z_i = 1$ if patient $i$ is assigned to the new treatment, and $z_i = 0$ if patient $i$ is assigned to the control treatment. Suppose that patients have been stratified or subclassified into one of $J$ strata on the basis of observed covariates, and that patient $i$ falls in stratum $s_i$. The population model for the stratifying variable $s$ is assumed to be a saturated multinomial.

In a stratified randomized trial, treatment assignment $z_i$ and response $(r_{1i}, r_{0i})$ are known to be conditionally independent given the stratum $s_i$, or in Dawid's (1979) notation:

$$(r_{1i}, r_{0i}) \perp\!\!\!\perp z_i \mid s_i \quad ; \qquad (1.2)$$

i.e., within strata, treatment assignment is "random". Condition (1.2) is not known to hold in a nonrandomized experiment. Generally, we shall say treatment assignment is <u>strongly ignorable given some set of covariates</u> $\underline{v}$ if

$$(r_{1i}, r_{0i}) \perp\!\!\!\perp z_i \mid \underline{v}_i \quad .$$

For brevity, when treatment assignment is strongly ignorable given the observed covariates (i.e., when as in a randomized experiment, (1.2) holds), we shall say simply that <u>treatment assignment is strongly ignorable</u>. (Technical Note: If treatment assignment is strongly ignorable, then it is ignorable in Rubin's (1978) sense, which only requires that the probabilities be evaluated at observed outcomes; however, the reverse is not true since strongly ignorable implies the relationship among probabilities must hold for all possible values of the random variables.)

We develop and apply a method to aid in judging the sensitivity of conclusions to certain plausible variations in assumptions about an unobserved binary covariate $u$. In particular, we assume that treatment assignment is not strongly ignorable given $s$, but is strongly ignorable given $s$ and

u; i.e., that (1.2) is false, but instead that

$$(r_{1i}, r_{0i}) \perp\!\!\!\perp z_i \mid s_i, u_i \tag{1.3}$$

is true. If conclusions are insensitive over a range of plausible assumptions about u, the number of interpretations of the data is reduced, and causal conclusions are more defensible.

## 2. AN EXAMPLE USING DATA ON CORONARY ARTERY DISEASE

Before presenting the model underlying the sensitivity analysis, we show the results of applying it to an example concerning symptomatic relief from coronary artery disease.* Treatment 1 is coronary artery bypass surgery; treatment 2 is medical therapy. The response $(r_1, r_0)$ is functional improvement six months after cardiac catheterization, with $r_t = 1$ signifying improvement under treatment $t$, $t = 0, 1$, and $r_t = 0$ signifying no improvement.

Here, patients are stratified by the multivariate method described in Rosenbaum and Rubin (1981) that balances 74 observed covariates. The observed proportion improved within each stratum is displayed in Table 1. In examining this table, it must be remembered that there exists evidence for a placebo effect of bypass surgery (Benson and McCalie (1979)).

When treatment assignment is strongly ignorable given the stratum $s$, then direct adjustment with stratum total weights yields the maximum likelihood estimate of the average treatment effect (1.1) under the saturated multinomial model for $s$. The directly adjusted proportions improved are .36 for medicine and .67 for surgery, with standard errors .04 and .05 respectively (calculated following Mosteller and Tukey, 1977, ch. 11c).

In order to study the sensitivity of estimates to the assumption of strongly ignorable assignment (i.e. to assumption (1.2)), we now assume that treatment assignment is not strongly ignorable, but rather that treatment assignment is strongly ignorable given $s$ and $u$ (i.e. that assumption (1.3) holds), where $u$ is an unobserved binary covariate. Table 2 displays the sensitivity of the estimate of the average treatment effect to 12 sets of assumptions about $u$. The method used to derive Table 2, and the symbols that appear in Table 2, will be mathematically defined in the next section.

---

* The data are used to illustrate methodology, and do not constitute a study of coronary artery disease.

Table 1

Proportion of Patients Improved at 6 Months In Each Stratum

| Stratum* | Treatment | Number of Patients | Proportion Improved | Standard Error |
|---|---|---|---|---|
| 1 | Medical | 277 | .35 | .03 |
| | Surgical | 26 | .54 | .10 |
| 2 | Medical | 235 | .40 | .03 |
| | Surgical | 68 | .70 | .06 |
| 3 | Medical | 205 | .35 | .03 |
| | Surgical | 98 | .70 | .05 |
| 4 | Medical | 139 | .30 | .04 |
| | Surgical | 164 | .71 | .04 |
| 5 | Medical | 69 | .39 | .06 |
| | Surgical | 234 | .70 | .03 |

* The strata were constructed by the method of Rosenbaum and Rubin (1981) in which the conditional probability of surgical treatment given the observed covariates is estimated, and patients with similar estimated probabilities are placed in the same stratum. The strata are predictive of treatment assignments; they are not prognostic strata. This method balances observed covariates within each stratum.

Roughly speaking, $\alpha$ is the increase in the log odds of surgery associated with $u = 1$ rather than $u = 0$; $\delta_t$ is the increase in the log odds of improvement under treatment $t$ associated with $u = 1$; and $\pi$ defines the marginal distribution of $u$ by $\pi = p(u=0)$.

In Table 2, the estimates of the proportion improved vary from .34 to .38 for medicine and from .63 to .70 for surgery; this range of values is about the same as the standard error of the directly adjusted proportions (i.e., .04 for medicine, .06 for surgery). Consequently, we see that this hypothetical, unobserved covariate $u$, which has defied the cardiologists' attempt to record all variables used in assigning treatments, would have to more than triple the odds of surgery and more than triple the odds of improvement, before altering the conclusion that the proportion improved under surgery far exceeds the proportion improved under medicine. Although this difference may reflect a placebo effect of surgery, the difference does not seem to be easily explained as the result of an imbalance due to the nonrandomized nature of the study.

Another way of describing this analysis is to say that we have explored the extent to which the data might be an example of Simpson's paradox. For discussion from this perspective, see Lindley and Novick (1981).

Table 2

**Effects of an Unobserved Two-Category Variable u on the Probability of Substantial Improvement at 6 Months for Medical (M) and Surgical (S) Patients**

| Effect of u=1 vs u=0 on Treatment Assignment z | Effect of u=1 vs u=0 on Improvement $r_t$ | Fraction of patients with u=0 (i.e. π) .1 | .5 | .9 |
|---|---|---|---|---|
| doubles the odds of surgery $\exp(\alpha) = 2$ | halves the odds of improvement $\exp(\delta_t) = .5$ | M .36<br>S .67 | M .35<br>S .68 | M .36<br>S .68 |
| .. | doubles the odds of improvement $\exp(\delta_t) = 2$ | M .36<br>S .66 | M .37<br>S .65 | M .36<br>S .66 |
| triples the odds of surgery $\exp(\alpha) = 3$ | reduces by 2/3 the odds of improvement $\exp(\delta_t) = 1/3$ | M .35<br>S .68 | M .34<br>S .70 | M .35<br>S .69 |
| | triples the odds of improvement $\exp(\delta_t) = 3$ | M .37<br>S .66 | M .38<br>S .63 | M .37<br>S .65 |

## 3. THE MODEL AND THE MAXIMUM LIKELIHOOD ESTIMATE

This section describes the model underlying the sensitivity analysis in Table 2; section 4 describes computational procedures. The principal result of this section is the derivation of the maximum likelihood estimate of the average treatment effect (1.1).

Assume treatment assignment is strongly ignorable given $s$ and $u$ (i.e., assume (1.2)). Let $\pi$ define the marginal distribution of the unobserved covariate $u$ by

$$p(u=0) = \pi$$

$$p(u=1) = 1 - \pi$$

where for convenience $u$ is assumed independent of $s$; i.e.,

$$u \perp\!\!\!\perp s \quad . \tag{3.1}$$

As stated previously, the population distribution of the stratifying variable is assumed to be a saturated multinomial for the $J$ possible values of $s$. Assume, for treatment assignment

$$p(z|s,u) = \frac{\exp\{z(\gamma_s + \alpha u)\}}{1 + \exp\{\gamma_s + \alpha u\}} \quad , \tag{3.2}$$

and assume for response under treatment $t$, $t = 1,2$

$$p(r_t=1|s,u) = \frac{\exp\{r_t(\beta_{st} + \delta_t u)\}}{1 + \exp\{\beta_{st} + \delta_t u\}} \quad , \tag{3.3}$$

where $\gamma_s$, $\beta_{st}$, $s = 1,\ldots,J$, $t = 0,1$, are parameters to be estimated, and $\alpha$, $\delta_0$, $\delta_1$, $\pi$ are parameters assigned values for the sensitivity analysis.

In words, the parameter $\alpha$ defines the relationship between the unobserved covariate $u$ and treatment assignment $z$; the parameter $\delta_t$ defines the relationship between $u$ and the response $r_t$ to treatment $t$, $t = 0,1$. Within every stratum, $u = 1$ increases the log odds of receiving treatment 1 by the same amount $\alpha$. Similarly, within every stratum, $u = 1$ increases the log odds of improvement under treatment $t$ (i.e., of $r_t = 1$) by the same amount $\delta_t$. (The development below can also be immediately applied to the case where $\pi$, $\delta_t$ and $\alpha$ are replaced by stratum dependent parameters $\pi_s$, $\delta_{st}$, and $\alpha_s$, which, in particular, do not satisfy assumption (3.1); however, this more general formulation introduces too many sensitivity parameters for many practical applications.)

For fixed values of the sensitivity parameters, $\alpha$, $\delta_0$, $\delta_1$, $\pi$, the maximum likelihood estimates (mle's) of the 3J parameters $\gamma_s$, $\beta_{s0}$, $\beta_{s1}$, $s = 1,2,\ldots,J$, do not have a simple, closed form. However, there are 3J parameters that are a 1-1 function of $\gamma_s$, $\beta_{s0}$, $\beta_{s1}$ that do have simple, explicit mle's, namely, $p(z=0|s)$, $p(r_0=0|z=0,s)$ and $p(r_1=0|z=1,s)$. We first derive the relationship between these two sets of parameters, then display the explicit mle's for the second set of parameters, and finally describe how to solve for the mle's of $\gamma_s$, $\beta_{s0}$, $\beta_{s1}$. Section 4 provides details for computing these solutions.

For $S = 1,\ldots,J$,

$$p(z=0|s) = \pi p(z=0|s, u = 0) + (1-\pi)p(z=0|s, u = 1)$$

$$= \frac{\pi}{1+\exp[\gamma_s]} + \frac{(1-\pi)}{1+\exp[\gamma_s+\alpha]} \quad . \tag{3.3}$$

Furthermore, using assumption (1.3) we have

$$p(r_t=0|z=t,\ s) = \tag{3.4}$$

$$p(r_t=0|s,\ u=0)p(u=0|z=t,\ s)$$

$$+\ p(r_t=0|s,\ u=1)p(u=1|z=t,\ s)$$

$$= \frac{w_{sz}}{1+e^{\beta_{st}}} + \frac{1-w_{sz}}{1+e^{\beta_{st}+\delta_t}}$$

$$w_{sz} = p(u=0|,z,s) = \frac{\dfrac{\pi\ \exp[z\gamma_s]}{1+\exp[\gamma_s]}}{\dfrac{\pi\ \exp[z\gamma_s]}{1+[\exp[\gamma_s]} + \dfrac{(1-\pi)\ \exp[z(\gamma_s+\alpha)]}{1+\exp[\gamma_s+\alpha]}} \tag{3.5}$$

$$= \frac{\pi}{\pi + (1-\pi)\ \dfrac{e^{z\alpha}[1+e^{\gamma_s}]}{1+e^{\gamma_s+\alpha}}}\ .$$

Note that the $w_{sz}$'s define the conditional distribution of the unobserved covariate $u$ given the observed treatment assignment.

Since $r_{ti}$ is observed only if $z = t$, the likelihood of the observed data is

$$\prod_{i=1}^{N} p(r_{ti}|z_i = t,\ s,\ \gamma_s,\ \beta_{st})p(z_i = t|s,\ \gamma_s)p(s)\ .$$

For specified $(\alpha,\ \delta_0,\ \delta_1,\ \pi)$, the model is saturated, so the mle's of $p(r_{ti}|z_i = t,\ s,\ \gamma_s,\ \beta_{st})$, $p(z_i = t|s,\ \gamma_s)$ and $p(s)$ are the corresponding observed proportions: the mle of $p(s = j)$ is the proportion $\hat{p}(s=j)$ of patients in stratum $j$, the mle of $p(z=0|s)$ is the observed proportion $\hat{p}(z = 0|s)$ of patients receiving treatment 0 in stratum $s$, and for $t = 0$

and 1, the mle of $p(r_t=0|z=t,s)$ is the observed proportion $\hat{p}(r_t = 0|z = t, s)$ of patients with response $r_t = 0$ among patients who received treatment $z = t$ in stratum $s$.

For each stratum $s$, equation (3.3) with $\hat{p}(z = 0|s)$ substituted for $p(z = 0|s)$ may be solved for the mle of $\gamma_s$, without reference to any other equation. Having found $\hat{\gamma}_s$ and calculated $\hat{w}_{st}$, equation (3.4) with $\hat{p}(r_t = 0|z = t,s)$ substituted for $p(r_t = 0|z = t,s)$ may be solved for $\hat{\beta}_{st}$ without reference to any other equation. Since equations (3.3) and (3.4) are of the same general form, a single one dimensional Newton-step algorithm yields maximum likelihood estimates of the parameters $\gamma_s$, $\beta_{s0}$, $\beta_{s1}$, $s = 1,\ldots,J$.

The mle of the average response to treatment $t$ in stratum $s$ is

$$\hat{p}(r_t=0|s)=\hat{p}(r_t=0|s,\ u=0)\pi + (1-\pi)\hat{p}(r_t=0|s,\ u=1)$$

$$= \frac{\pi}{1+e^{\hat{\beta}_{st}}} + \frac{1-\pi}{1+e^{\hat{\beta}_{st}+\delta_t}} .$$

Thus, the mle of the average response $\tau_t$ to treatment $t$ is given by the directly adjusted rate

$$\hat{\tau}_t = \sum_{j=1}^{J} \hat{p}(r_t=0|s=j)\hat{p}(s=j) \qquad (3.6)$$

where $\hat{p}(s=j)$ is the proportion of patients in stratum $j$. Values of the estimator $\hat{\tau}_t$ are displayed in Table 2 for our data and various assumptions about the sensitivity parameters $(\pi, \alpha, \delta_1, \delta_2)$.

## 4. MAXIMUM LIKELIHOOD COMPUTATIONS

Equations (3.3) and (3.4) are both of the form

$$p = \frac{a}{1+e^{\theta}} + \frac{1-a}{1+e^{\theta+b}} \quad . \tag{4.1}$$

To find $\theta$ for fixed $a$, $b$ and $p$, we use the following Gauss-Newton iteration

$$\theta_{n+1} = \theta_n + \frac{\dfrac{1-a}{1+e^{\theta_n+b}} + \dfrac{a}{1+e^{\theta_n}} - p}{\dfrac{(1-a)e^{\theta_n+b}}{(1+e^{\theta_n+b})^2} + \dfrac{a\, e^{\theta_n}}{(1+e^{\theta_n})^2}} \quad . \tag{4.2}$$

The iteration (4.2) can be easily programmed on a pocket calculator.

To calculate $(\hat{\gamma}_s, \hat{\beta}_{s0}, \hat{\beta}_{s1})$ for fixed $(\pi, \alpha, \delta_1, \delta_2)$:

a) Solve (3.3) for $\hat{\gamma}_s$ using (4.2) with $p = \hat{p}(z=0|s)$, $a = \pi$, $b = \alpha$.

b) For $t = 0,1$ find $\hat{w}_{st}$ using (3.5).

c) For $t = 0,1$ solve (3.4) for $\hat{\beta}_{st}$ using (4.2) with $p = \hat{p}(r_t=0|z=t,s)$, $a = \hat{w}_{st}$, $b = \delta_t$.

Steps a, b, and c are repeated for $S = 1,\ldots,J$ and the results combined using (3.6).

Although the iteration (4.2) can easily be performed using a hand calculator, a simple closed form approximation is convenient for obtaining a good starting value, especially if many sensitivity analyses are to be performed. Specifically, the solution $\theta$ of equation (4.1) can be closely approximated by a Taylor approximation, providing $.05 \leq p \leq .95$.

Define $L$ as the logit

$$L = \log_e \frac{1-p}{p}$$

so

$$\frac{1}{1+e^{L}} = p \quad .$$

Equation (4.1) may be rewritten

$$0 = \frac{a}{1+e^{\theta}} + \frac{1-a}{1+e^{\theta+b}} - \frac{1}{1+e^{L}} \quad . \tag{4.3}$$

Implicit differentiation (e.g., Hildebrand (1962), page 339) of (4.3) yields

$$\frac{\partial \theta}{\partial p} = \frac{\dfrac{e^{L}}{(1+e^{L})^{2}}}{\dfrac{ae^{\theta}}{(1+e^{\theta})^{2}} + \dfrac{(1-a)e^{\theta+b}}{(1+e^{\theta+b})^{2}}} \quad .$$

AT $\theta = 0$, $p$ equals

$$\frac{a}{2} + \frac{1-a}{1+e^{b}} = p_0 \quad , \quad \text{say}$$

and therefore $L$ equals

$$\log_e \frac{1-p_0}{p_0} = L_0 \quad , \quad \text{say} \quad .$$

Expanding around $L_0$ yields the closed form approximation

$$\theta = \frac{\dfrac{e^{L_0}}{(1+e^{L_0})^{2}}}{\dfrac{a}{4} + \dfrac{(1-a)e^{b}}{(1+e^{b})^{2}}} \, (L-L_0) \quad . \tag{4.4}$$

## REFERENCES


Bensen and McCallie (1979). Angina pectoris and the placebo effect. New England Journal of Medicine, 300:1424-1428.

Bross, I. D. J. (1966). Spurious effects from an extraneous variable. Journal of Chronic Diseases, 19:637-647.

Cornfield, J., et. al. (1959). Smoking and lung cancer: Recent evidence and a discussion of some questions. Journal of the National Cancer Institute, 22:173-200.

Cox, D. R. (1958). The Planning of Experiments. New York: John Wiley and Sons.

Dawid, A. (1979). Conditional independence in statistical theory (with discussion). Journal of the Royal Statistical Society, Series B, 41:1-31.

Fisher, R. A. (1953). The Design of Experiments. London: Hafner.

Hamilton, M. A. (1979). Choosing a parameter for a 2 × 2 table or 2 × 2 × 2 table analysis. American Journal of Epidemiology, 109:362-375.

Kempthorne, O. (1952). The Design and Analysis of Experiments. New York: John Wiley.

Lindley, D. V. and Novick, M. R. (1981). The role of exchangability in inference. Annals of Statistics, 9:45-58.

Mosteller, C. F. and Tukey, J. W. (1977). Data Analysis and Regression, Reading, Mass., Addison-Wesley.

Rosenbaum, P. R. and Rubin, D. B. (1981). The central role of the propensity score in observational studies for causal effects. Submitted to Biometrika.

Rubin, D. B. (1977). Assignment to treatment group on the basis of a covariate. Journal of Educational Statistics, 2:1-26.

Rubin, D. B. (1978). Bayesian inference for causal effects: the role of randomization. Annals of Statistics, 6:34-58.

PRR/DBR/jvs

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

| REPORT DOCUMENTATION PAGE | READ INSTRUCTIONS BEFORE COMPLETING FORM |
|---|---|
| 1. REPORT NUMBER #2321 | 2. GOVT ACCESSION NO. AD-A114 478 |
| 3. RECIPIENT'S CATALOG NUMBER | |
| 4. TITLE (and Subtitle) Assessing Sensitivity to an Unobserved Binary Covariate in a Nonrandomized Experiment with Binary Outcome | 5. TYPE OF REPORT & PERIOD COVERED Summary Report - no specific reporting period |
| | 6. PERFORMING ORG. REPORT NUMBER |
| 7. AUTHOR(s) Paul R. Rosenbaum and Donald B. Rubin | 8. CONTRACT OR GRANT NUMBER(s) MRA 230-76-0300 DAAG29-80-C-0041 P30-CA-14520 |
| 9. PERFORMING ORGANIZATION NAME AND ADDRESS Mathematics Research Center, University of Wisconsin 610 Walnut Street Madison, Wisconsin 53706 | 10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS Work Unit Number 4 - Statistics & Probability |
| 11. CONTROLLING OFFICE NAME AND ADDRESS (see Item 18 below) | 12. REPORT DATE January 1982 |
| | 13. NUMBER OF PAGES 16 |
| 14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office) | 15. SECURITY CLASS. (of this report) UNCLASSIFIED |
| | 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE |

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

U. S. Army Research Office
P. O. Box 12211
Research Triangle Park
North Carolina 27709

National Cancer Institute
9000 Rockville Pike
Bethesda, MD 20205

Health Resources Administration
3700 East-West Highway
Hyattsville, MD 20782

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Observational studies, sensitivity analysis, categorical data

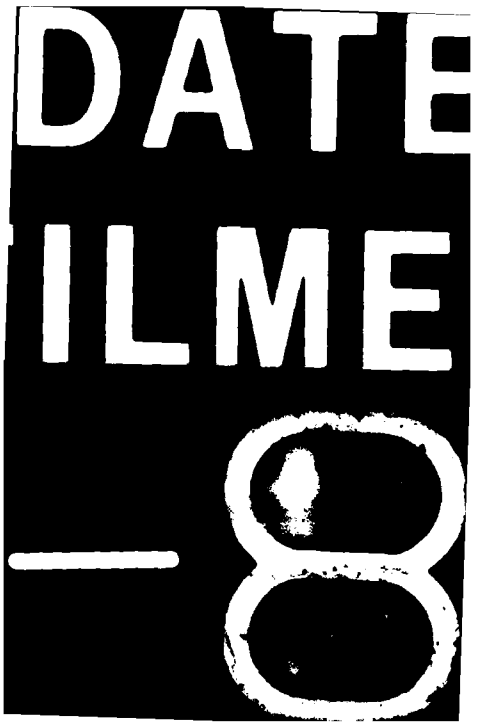
20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The results of nonrandomized clinical experiments are often disputed because patients at greater risk may be overrepresented in some treatment groups. This paper proposes a simple technique providing insight into the range of plausible conclusions from a nonrandomized experiment with binary outcome and categorical covariate. The technique assesses the sensitivity of conclusions to assumptions about an unobserved binary covariate relevant to treatment assignment, and is illustrated in a medical study of coronary artery disease.

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)


DATE
ILME
8